RELEVANCE OF SYSTEMIC IMMUNOSUPPRESSION IN OVARIAN CANCER PATIENTS

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Introduction: Ovarian cancer is a silent killer, metastasising throughout the abdomen before causing symptoms. This immediately explains that mortality (which is the case in 80% of patients) is caused by the metastases. So far, research concerning the immune system in ovarian cancer has focussed on the tumor microenvironment. The peripheral immune landscape in ovarian cancer remains largely undiscovered.

Material and method: Peripheral blood mononuclear cells were collected prospectively in 39 patients with invasive ovarian cancer. Samples were prelevated at diagnosis, after cytoreductive surgery ((interval-)debulking), after three courses of (neo-)adjuvant platin-based chemotherapy, and at the end of their primary treatment. Fluorescent activated cell sorting was applied to detect immunostimulatory cells (T_{helper} cells ($CD4^+$), $T_{cytotoxic}$ cells ($CD8^+$), natural killer cells (NK)) and immunosuppressive cells (regulatory T cells (Treg), mMDSC (monocytic myeloid-derived suppressor cells), gMDSC (granulocytic MDSC)).

Results and discussion: Patients were distributed as follows: 76% had an advanced stage of the disease at diagnosis (stage III and IV), 44% relapsed, including six deaths. Tumors had a high-grade histology in 80% of cases. Stage IV ovarian cancers presented with higher amounts of mMDSC (p 0.007). High-grade ovarian cancers presented with more $PD1^+$MDSC (p 0.03) (PD1 = programmed cell death protein 1). After primary treatment (i.e. chemotherapy and debulking surgery) there was an increase of $T_{cytotoxic}$ cells (p 0.002) and activated $T_{cytotoxic}$ cells ($CD8^+CD69^+$) (p 0.02) T cells. Debulking surgery increased the number of activated T_{helper} cells ($CD4^+CD69^+$) (p 0.02). Progression free survival was significantly reduced in case of increasing amount of T_{helper} cells (p 0.02), activated T_{helper} cells (p 0.002), activated $T_{cytotoxic}$ cells (p 0.01), mMDSC (p 0.03) and $PD1^+$mMDSC (p 0.002). Overall survival was reduced in case of increasing activated T_{helper} cells (p 0.04) and activated $T_{cytotoxic}$ cells (p 0.04).

Conclusion: In contrast to what is seen in literature in the primary tumor, a high presence of T_{helper} cells and $T_{cytotoxic}$ cells in the systemic circulation of ovarian cancer patients is correlated with a worse survival. It almost seems that the systemic immune system represents a state of immune alert of the body as a reaction to widespread metastatic disease but that this is insufficient. mMDSC seem to be an important immunosuppressive player in ovarian cancer.